REMARKS

I. Status of the claims

Claims 9-20 and 22-38 are currently pending. New claims 22-38 are supported by the specification and do not contain new matter.[1]

II. Rejection of claims 9-20 under 35 U.S.C. § 102 (b) or (e)

Reconsideration is requested of the rejection of claims 9-20 under § 102(b) or (e) as anticipated by Isakson et al.[2] ("Isakson I"); Isakson et al.[3] ("Isakson II"), Isakson et al.[4] ("Isakson III"), Gregory et al.[5]; Engelhardt et al.[6], Talley et al.[7], Hagmann et al.[8], Mills et al.[9], and Finke et al.[10]

A. The Cited Art is not Available to Support a Rejection of Claims 9-20 under 35 U.S.C. § 102(e)

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[1]For cyclooxygenase-2 inhibitors see pages 17-18 of the specification. For 5-lipoxygenase inhibitors see pages 13-15 of the specification. For cyclosporin compounds, see page 3 of the specification.

[2]U.S. Patent No. 6,136,839.

[3]U.S. Patent No. 5,990,148.

[4]WO 96/41626.

[5]U.S. Patent No. 6,407,140.

[6]Chem. Abst. 125:292089.

[7]U.S. Patent No. 5,859,257.

[8]U.S. Patent No. 4,919,776.

[9]U.S. Patent No. 6,013,644.

[10]U.S. Patent No. 6,500,844.

For the reasons detailed below, the art cited by the Office may not properly be used to support a 35 U.S.C. § 102(e) rejection of claims 9-20.

According to the Office, the instant application is to be examined under 35 U.S.C. §102(e) as it existed prior to the amendment by the American Inventors Protection Act of 1999, because "the application was not filed on or after November 29, 2000 or voluntarily published under § 122(b)."[11] This statement is incorrect. 35 U.S.C. §102(e) has been amended by the enactment of H.R. 2215, the Intellectual Property and High Technology Technical Amendments Act of 2002. In accordance with this amendment, MPEP § 2136 specifically dictates:

> ...revised 35 U.S.C. § 102(e), as amended by the American Inventors Protection Act of 1999 (AIPA) (Pub. L. 106-113, 113 Stat. 1501 (1999)), and as further amended by the Intellectual Property and High Technology Technical Amendments Act of 2002 (Pub. L. 107-273, 116 Stat. 1758 (2002)), applies in the examination of all applications, **whenever filed**...Thus, the **filing date** of the application being examined is **no longer relevant** in determining what version of 35 U.S.C. § 102(e) to apply in determining the patentability of that application or the patent resulting from that application. The revised statutory provisions supercede all previous versions of 35 U.S.C. § 102(e).[12]

The analysis provided below by applicants regarding whether the references cited by the Office may properly be cited in support of its § 102(e) rejection of claims 9-20 is consistent with the amendment of § 102(e) via H.R. 2215.

35 U.S.C § 102(e) specifically dictates that a person shall be entitled to a patent unless the invention was described in "a patent granted on an application for patent by another filed in the United States **before** the invention by the applicant for patent."[13]

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[11]See Paper 9 at page 2.

[12]See the First Revision to the Eight Edition of the MPEP § 2136 (emphasis added).

[13]35 U.S.C. §102(e)(2) (emphasis added).

The present application has an effective filing date of **February 13, 1996**: although filed on March 15, 2002, the present application is a divisional of application Serial No. 09/430,072 (now U.S. Patent No. 6,376,528), filed October 18, 1999, which was a continuation of application Serial No. 09/189,463 (now abandoned), filed November 10, 1998, which was a continuation of Serial No. 08/600,622 (now abandoned) filed February 13, 1996.

According to the face of the Hagmann et al. patent, the patent claims priority from provisional application Serial No. 60/033,536 ('536), filed December 20, 1996. Thus, Hagmann et al. is at most entitled to the filing date of the '536 application, i.e., December 20, 1996, more than eight months after the effective filing date of the present application.

The Finke et al. patent claims priority from provisional application Serial No. 60/139,067 ('067), filed June 11, 1999. Therefore, Finke et al. is at most entitled to the filing date of the '067 application, i.e., June 11, 1999, more than 3 years after the effective filing date of the current application.

According to the face of the Mills et al. patent, the patent claims priority from two provisional applications: provisional application Serial No. 60/032,890 ('890), filed December 13, 1996 and 60/033,535 ('535), filed December 20, 1996. Accordingly, Mills et al. at most is entitled to the filing date of the '890 application, i.e., December 13, 1996, more than eight months after the effective filing date of the present application.

According to the face of the Gregory et al. patent, the patent was a continuation of application Serial No. 08/600,655 (now abandoned), filed February 13, 1996. Therefore, Gregory et al. has a filing date of February 13, 1996, the **same day** as the effective filing date of the current application.

Because each of the Hagmann et al., Finke et al., Mills et al., and Gregory et al. patents have effective filing dates that are either before or on the same day as the effective filing date of the current application, they cannot properly be used to support a 35 U.S.C. § 102(e) of claims 9-20.

Isakson I et al. and Isakson II et al. were each filed June 11, 1996. Isakson I et al. is a continuation-in-part of application Serial No. 08/489,472 (now abandoned), which was filed June 12, 1995, and Isakson II et al. is a continuation-in-part of application Serial No. 08/489,468 (now U.S. Patent No. 5,700,816), which was filed June 12, 1995. In addition, the Talley et al. patent was filed August 14, 1996 and ultimately claims priority from an application that is a continuation-in-part of application Serial No. 387,680 (now abandoned), which was filed February 13, 1995. MPEP § 2136.03(IV) specifically states that the "filing date of a parent application [when the reference is a continuation-in-part of the parent] can only be used as the 35 U.S.C. § 102(e) date if it supports the claims of the issued child." No showing has been made by the Office that the respective parent application in each of Isakson I et al., Isakson II et al. or Talley et al. support the claims of the issued child (i.e., Isakson I et al., Isakson II et al., or Talley et al.) as required by MPEP § 2136.03(IV). Without this showing, Isakson I et al., Isakson II et al. and Talley et al. cannot properly be cited by the Office to support a 35 U.S.C. § 102(e) rejection of claims 9-20.

Isakson III et al. is a WIPO publication of an international application with an international filing date of June 11, 1996. Pursuant to MPEP § 2136.03(II), a WIPO publication of an international application filed prior to November 29, 2000, may not properly be used to support a 35 U.S.C. § 102(e) rejection.

Engelhardt et al. is a journal article published in 1996. In accordance with 35 U.S.C. § 102(e), journal articles, irrespective of their date of publication, may not be used to support a 35 U.S.C. § 102(e) rejection of claims 9-20.

In view of the above, applicants respectfully request a withdrawal of the rejection of claims 9-20 under 35 U.S.C. § 102(e).

B. The Cited Art is not Available to Support a Rejection of Claims 9-20 under 35 U.S.C. § 102(b)

For the reasons detailed below, the art cited by the Office may not properly be used to support a 35 U.S.C. § 102(b) rejection of claims 9-20.

MPEP § 706.02(a) specifically dictates "if the publication or issue date of the reference [used in a 102(b) rejection] is more than 1 year prior to the effective filing date of the application, the reference qualifies as prior art under 35 U.S.C. § 102(b)."[14]

In this case, as detailed in II.A., the effective filing date of the present application is **February 13, 1996.** Consistent with MPEP § 706.02(a), to qualify as prior art against the present application under § 102(b), a reference must have an issue or publication date on or before **February 12, 1995**. According to the face of each of the Isakson I et al., Isakson II et al., Gregory et al., Hagmann et al., Finke et al., Mills et al., and Talley et al. patents the issue dates were October 24, 2000, November 23, 1999, June 18, 2002, July 6, 1999, December 31, 2002, January 11, 2000, and January 12, 1999, respectively. According to the face of Isakson III et al., its international publication date was December 27, 1996. Moreover, the Engelhardt et al. journal article was published in 1996. None of the references cited by the Office were published or issued on or before February 12, 1995. The references, therefore, **are not** prior art under 35 U.S.C. § 102(b).

In view of the above, Applicants respectfully request a withdrawal of the rejection of claims 9-20 under 35 U.S.C. § 102(b).

C. The cited art does not anticipate the combination of claims 9-20

Claim 9 is directed toward a composition comprising a **cyclooxygenase-2 inhibitor** (COX-2), a **5-lipoxygenase inhibitor** (5-LO) and an **immunosuppressive drug** selected from antiproliferative agents, antiinflammatroy-acting compounds and inhibitors of leukocyte activation.

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[14]Also see 35 U.S.C. § 102(b).

Isakson I et al. and Isakson III et al. each disclose combinations and compositions comprising a COX-2 inhibitor and a 5-LO inhibitor. As noted by the Office, the cited art discloses that the pharmaceutical compositions may further comprise a pharmaceutically-acceptable carrier, diluent and/or adjuvant, "and, if desired, other active ingredients."[15] But nowhere do Isakson I et al. or Isakson III et al. disclose or suggest that the "other active ingredient" should be an **immunosuppressive drug**, as required by claim 9.

Gregory et al. disclose combinations comprising a COX-2 inhibitor, **a leukotriene A_4 hydrolase** (LTA_4) inhibitor, and an immunosuppressive agent. Claim 9 requires a 5-LO inhibitor not a LTA_4 inhibitor. 5-LO inhibitors are not the same as LTA_4 inhibitors.[16] Arachidonic acid may be oxygenated via either the cyclooxygenase pathway (to produce prostaglandins) or via the lipoxygenase pathway (to produce leukotrienes). 5-LO converts arachidonic acid to leukotriene A_4 (LTA_4), which is then converted to LTB_4 by the LTA_4 hydrolase enzyme. Thus, an LTA_4 inhibitor is different from a 5-LO inhibitor, in that the latter prevents the formation of LTA_4 from arachidonic acid, while the former prevents the conversion of LTA_4 to LTB_4.

Isakson II et al. disclose combinations comprising a COX-2 inhibitor and **a leukotriene A_4 hydrolase** (LTA_4) inhibitor. Isakson II et al. do not disclose a combination of COX-2 inhibitors, 5-LO inhibitors and an immunosuppressant, as required by claim 9.

Engelhardt et al. describe findings of a non-steroidal anti-inflammatory drug (NSAID), meloxicam. The abstract does disclose that meloxicam preferentially inhibits COX-2 leukocyte migration. But nowhere do Engelhardt et al. disclose the combination of COX-2 inhibitors, 5-LO inhibitors and an immunosuppressant, as required by claim 9.

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[15]See Isakson I, col. 31, line 46-51; Isakson II, page 46, line 27-33.

[16]See Isakson I, col. 1, lines 21-55.

Talley et al. disclose combinations comprising a COX-2 inhibitor and a 5-LO inhibitor. But they do not disclose a combination of COX-2 inhibitors, 5-LO inhibitors and an immunosuppressant, as required by claim 9.

Hagmann et al. disclose a class of substituted aminoquinolines that modulate chemokine receptor activity for use in the treatment of certain inflammatory and immunoregulatory disorders. Although Hagmann et al. disclose that their substituted aminoquinolines may be used in combination with **a** COX-2 inhibitor, **or a** 5-LO inhibitor, **or an** immunosuppressant, they do not disclose or suggest a combination having a COX-2 inhibitor along with a 5-LO inhibitor and an immunosuppressant, as required by claim 9.

Finke et al. disclose a class of substituted cyclopentyl compounds that modulate chemokine receptor activity that prevent the entry of HIV into a cell. Finke et al. do disclose that their substituted cyclopentyl compounds may be used in combination with **a** COX-2 inhibitor, **or a** 5-LO inhibitor, **or an** immunosuppressant. But nowhere do they disclose or suggest a combination having a COX-2 inhibitor along with a 5-LO inhibitor and an immunosuppressant, as required by claim 9.

Mills et al. disclose a class of spiro-substituted azacycles that modulate chemokine receptor activity for use in the treatment of certain inflammatory and immunoregulatory disorders. Although Mills et al. disclose that their substituted aminoquinolines may be used in combination with **a** COX-2 inhibitor, **or a** 5-LO inhibitor, **or an** immunosuppressant, they do not disclose or suggest a combination having a COX-2 inhibitor along with a 5-LO inhibitor and an immunosuppressant, as required by claim 9.

None of the art cited by the Office discloses a combination with the components of the claim 9 composition. A claim is anticipated only if each and every element as set

forth in the claim is described in a single prior art reference.[17] Because the cited art does not disclose every element of claim 9, the references do not anticipate claim 9. Claims 10-20 depend from claim 9, and are likewise patentable over these references for the reasons stated with respect to claim 9. Moreover, each of claims 10-20 and new claims 22-38 require COX-2 inhibitors, 5-LO inhibitors, and immunosuppressants having a specific recited chemistry that is not disclosed in the cited art.

III. Rejection of claims 9-20 under 35 U.S.C. § 103(a)

Reconsideration is requested of the rejection of claims 9-20 under § 103(a) as obvious in view of Isakson I et al., Isakson II et al., Isakson III et al., Gregory et al., Engelhardt et al., Talley et al., Hagmann et al., Mills et al., and Finke et al.

A. The Cited Art is not Available to Support a Rejection of Claims 9-20 under 35 U.S.C. § 103(a)

In order to qualify as prior art to support a §103(a) rejection, each reference cited must qualify as prior art under 35 U.S.C. § 102.[18] According to the Office, Isakson I et al., Isakson II et al., Isakson III et al., Gregory et al., Engelhardt et al., Talley et al., Hagmann et al., Mills et al., and Finke et al. qualify as prior art under § 102(b) and/or (e). As detailed in II A. and II.B, however, none of the references may properly be used to support a § 102(b) or (e) rejection of claims 9-20 and concomitantly, also may not be used to support a §103(a) rejection.

Moreover, effective November 29, 1999, 35 U.S.C. § 103(c) provides that subject matter which qualifies under 35 U.S.C.§ 102(e) **is not** to be considered when determining whether an invention sought to be patented is obvious under 35 U.S.C.

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[17]Verdegaal Bros. v. Union Oil Co. of Calif., 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987). See MPEP §2131.

[18]See MPEP § 2144(II)(A)(1).

§ 103, provided the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. Both the instant application and the Isakson I et al., Isakson II et al., Gregory et al., and Talley et al. patents have been assigned to G.D. Searle & Co.[19] In light of this common assignment, Isakson I et al., Isakson II et al., Gregory et al., and Talley et al. are unavailable to support a rejection of claims 9-20 under 35 U.S.C. § 103.

Accordingly, the rejection of claims 9-20 under 35 U.S.C. § 103(a) as obvious over Isakson I et al., Isakson II et al., Isakson III et al., Gregory et al., Engelhardt et al., Talley et al., Hagmann et al., Mills et al., and Finke et al. is improper.

B. The cited art does not render the combination of claims 9-20 obvious

As detailed in II C, the cited art taken singly does not disclose or suggest each element of the combination of claim 1. Moreover, as detailed in II C, the cited art taken collectively does not disclose or suggest a combination having the components of the claim 9 composition.[20]

According to the Office, combining the disclosure of "Isakson" with the disclosure of Hagmann et al. renders claim 9 obvious because "Isakson" is said to disclose "the combination of COX-2, 5-LO and antinflammatory compounds" and Hagmann is said to disclose a class of compounds that "modulate chemokine receptor activity and are used

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[19]Applicants can submit copies of the assignment documents for the each patent and the instant application upon request.

[20]Paper 9 at page 3 states that claims 9-20 remain rejected in view of the cited art for the reasons stated in Paper 5 dated February 11, 2003. Applicants' response regarding the rejections detailed in Paper 5 are set forth in their response dated June 11, 2003. To avoid duplication, Applicants have only addressed new grounds of rejection cited by the Office in Paper 9 with this response.

to treat inflammatory and immunoregulatory disorders."[21] This is not correct. Moreover, the Office does not specify which of the Isakson references, Isakson et al. I, II and III it is relying upon (as a result, each Isakson reference is addressed below). But irrespective of which Isakson et al. reference is combined with Hagmann et al., these references, taken singly or together, provide no basis for the Office's conclusion.

Among the many compounds disclosed in each of Isakson et al. I, II, or III and Hagmann et al., no reference offers any guidance that would have enabled a skilled artisan to prepare the combination employed in the method of claim 9. Isakson et al. I and III disclose combinations and compositions comprising a COX-2 inhibitor and a 5-LO inhibitor. Isakson et al. II discloses a combination of a COX-2 inhibitor and a **leukotriene A_4 hydrolase inhibitor**. Each of Isakson et al. I, II, and III disclose that the combination (i.e., COX-2 inhibitor and 5-LO inhibitor or COX-2 inhibitor and LTA_4 inhibitor) may further comprise a pharmaceutically-acceptable carrier, diluent and/or adjuvant, "and, if desired, other active ingredients."[22] But nowhere do Isakson et al. I, II, or Isakson III et al. disclose or suggest that the "other active ingredient" should be an **immunosuppressive drug**, as required by the claim 9 combination. Hagmann et al. disclose a class of substituted aminoquinolines that modulate chemokine receptor activity for use in the treatment of certain inflammatory and immunoregulatory disorders and in particular, HIV infections. Hagmann et al. disclose that their substituted aminoquinolines may be used in combination with a laundry list of approximately 150 other compounds.[23] Hagmann et al. specifically disclose:

> ...for example, in the treatment or prevention of inflammation, the present compounds [aminoquinolines] may be used in conjunction with an antiinflammatory **or** analgesic agent such as an opiate agonist, a

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[21]Paper 9 at page 3.

[22]See Isakson I, col. 31, line 46-51; Isakson II, page 46, line 27-33.

[23]U.S. Patent No. 5,919,776, columns 12-17.

> lipoxygenase inhibitor, such as an inhibitor of 5-lipoxygenase, a cyclooxygenase inhibitor, such as a cyclooxygenase-2 inhibitor...[24]

Accordingly, Hagmann et al. suggest that their aminoquinolines may be combined with **a** COX-2 inhibitor, **or a** 5-LO inhibitor, **or an** immunosuppressant as **alternative embodiments**. Based upon the Hagmann et al. disclosure, a skilled artisan may combine an aminoquinoline with a COX-2 inhibitor, or an aminoquinoline with a 5-LO inhibitor, or an aminoquinoline with an immunosuppressant. But contrary to the Office's assertion, a skilled artisan would not be motivated to combine a COX-2 inhibitor, a 5-L0 inhibitor and an immunosuppressant to arrive at the composition employed of claim 9. Moreover, a skilled artisan empowered with the cited art cannot fairly be deemed to be motivated to select a COX-2 inhibitor and a 5-LO inhibitor disclosed in the either of Isakson et al. I or III and combine it with the numerous variations of compositions disclosed in Hagmann et al. to form the composition recited in claim 9. As stated in MPEP 2143, where there is no motivation to modify a reference as proposed, the proposed modification is not obvious.

Further, the Office has provided no reason or rationale as to why a skilled artisan would be motivated to combine the disclosure of **nine separate** references: Isakson I et al., Isakson II et al., Isakson III et al., Gregory et al., Engelhardt et al., Talley et al., Hagmann et al., Mills et al., and Finke et al. For example, why would it have been obvious to modify the composition disclosed in Isakson et al. I or III et al. so as to include an immunosuppressive drug as allegedly disclosed by Engelhardt et al.? The Office merely delineates bare assertions regarding what each reference purportedly discloses and then concludes that claims 9-20 are obvious. To properly establish a *prima facie* case of obviousness, the law requires more than conclusions supported by bare assertions.

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[24] Id., column 12, lines 9-13 (emphasis added).

For the foregoing reasons, the Office has failed to establish that claim 9 is *prima facie* obvious in view of the cited art. Claims 10-20 depend from claim 9, and are likewise patentable over these references for the reasons stated with respect to claim 9. Moreover, each of claims 10-20 and new claims 23-38 require COX-2 inhibitors, 5-LO inhibitors, and immunosuppressants having a recited chemistry. Nowhere does the cited art, either alone or taken together, disclose or suggest combinations of compounds having the chemistry recited in each of claim 10-20 and 23-38.

IV. 35 U.S.C.112, First Paragraph Rejections

Reconsideration is requested of the rejection of Claims 9-20 under 35 U.S.C.112, first paragraph as not sufficiently enabled by the specification.

Claim 9 is directed toward a composition comprising a **cyclooxygenase-2 inhibitor** (COX-2), a **5-lipoxygenase inhibitor** (5-LO) and an **immunosuppressive drug** selected from antiproliferative agents, antiinflammatroy-acting compounds and inhibitors of leukocyte activation.

The standard for enablement is whether one of ordinary skill in the art could make or use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation.[25] In this case, the specification coupled with information generally known in the art, fully enables a skilled artisan to identify and prepare compositions for use in the present invention **without undue experimentation**.

The specification recites both functional and structural features that enable a skilled artisan to select suitable cyclooxygenase-2 inhibitors for use in the claim 9 combination. In terms of function, the specification defines a cyclooxygenase-2 inhibitor as:

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[25]U.S. v. Teletronics, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988).

> ...compounds which selectively inhibit cyclooxygenase-2 over cyclooxygenase-1. Preferably, the compounds have a cyclooxygenase-2 IC_{50} of less than about 0.5 μM, and also have a selectivity ratio of cyclooxygenase-2 inhibition over cyclooxygenase-1 inhibition of at least 50, and more preferably of at least 100. Even more preferably, the compounds have a cyclooxygenase-1 IC_{50} of greater than about 1 μM and more preferably of greater than 20 μM. Such preferred selectivity may indicate an ability to reduce the incidence of common NSAID-induced side effects.[26]

In terms of structure, the specification recites that the cyclooxygenase-2 inhibitor is selected from meloxicam, flosulide and a class of sulfonamides or methylsulfonyls compounds having formula I.[27] The specification further discloses 13 examples of compounds having formula I.[28] The specification also provides detailed guidance that fully enables a skilled artisan to prepare a cyclooxygenase-2 inhibitor employed in the combination of claim 9. According to the specification, any one of reaction schemes I-X may be utilized to prepare a cyclooxygenase-2 inhibitor having formula I.[29] The specification further discloses 3 examples of compounds that were made following the steps of one of the reaction schemes.[30]

Similarly, the specification recites both functional and structural features that enable a skilled artisan to select suitable 5-LO inhibitors for use in the claim 9 combination. In terms of function, the specification defines a 5-LO inhibitor as "compounds which selectively inhibit 5-lipoxygenase with an IC_{50} of less than about 10 μM. More preferably, the 5-lipoxygenase inhibitors have an IC_{50} of less than about 1

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[26]See page 12, lines 5-16, of the specification.

[27]See pages 12, and 15-18, of the specification.

[28]See pages 17-18 of the specification.

[29]See pages 27-40 of the specification.

[30]See pages 41-43 of the specification.

μM."[31] In terms of structure, the specification discloses well over 150 examples of publically available compounds having the recited function (i.e., selective 5-LO inhibition).[32]

In addition, the specification discloses a number of classes of immunosuppressants that may be employed in the combination of claim 9 along with examples of specific compounds belonging to each class. In particular, the specification states the immunosuppressant may be an antiproliferative agent, antiinflammatory-acting compound or an inhibitor of leukocyte activation selected from the following compounds:

> ...a cyclosporin compound, or Fujisawa FK-506 (macrolide lactone) compound, or rapamycin, or a glucocorticoid, or an antiproliferative agent, or a monoclonal antibody such as an anti-CD3 (anti-T cell receptor antibody) or anti-CD5/7 or anti-CD4 agent, or an anti-IL-2 receptor (anti-cytokine receptor type antibody) agent, or an anti-IL-2 (anti-cytokine antibody), or Nippon NKT-01 (15-deoxyspergualin) or Syntex RS-61443.[33]

The specification also details biological testing of an embodiment of the claim 9 composition in a "transplantation and evaluation of graft rejection" model.[34]

In view of the foregoing, a skilled artisan is fully empowered to make and use the combination of claim 9 without undue experimentation.

According to the Office, however, the specification does not enable a skilled artisan to "make the compounds" or to "identify" compounds because the only identifying characteristics "for recognizing that a compound is a candidate for the

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[31]See page 12, lines 17-21 of the specification.

[32]See pages 13-14 of the specification.

[33]See pages 11-12 of the specification.

[34]See pages 43-45 of the specification.

instant claims is the activity."[35] This is not correct. As detailed above, the specification recites **both** functional and structural features that enable a skilled artisan to select and make suitable cyclooxygenase-2 inhibitors, 5-LO inhibitors and immunosuppressants for use in the claim 9 combination. Patent applicants are not required to show a specific example for every possible embodiment of the claimed invention, so long as the specification and the general knowledge of the art would enable one of ordinary skill in the art to make and use the invention.[36] In this case, the specification along with the general knowledge of the art sufficiently enable a skilled artisan to make and use the combination of claim 9.

Claims 10-20 and new claims 23-38 incorporate all the claim 9 elements, and are likewise enabled for the reasons stated with respect to claim 9. Moreover, each of claims 10-20 and new claims 23-38 require COX-2 inhibitors, 5-LO inhibitors, and immunosuppressants having a recited chemistry such that a skilled artisan could make or use the composition in each of these claims without undue experimentation.

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[35]Paper 9 at page 4.

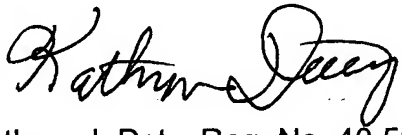
[36] In re Borkowski, 164 U.S.P.Q. 642, 645 (CCPA 1970).

V. Conclusion

In light of the foregoing, Applicants request an entry of the claim amendments, withdrawal of claim rejections and solicit an allowance of the claims. The Examiner is invited to contact the undersigned attorney should any issue remain unsolved.

A check in the amount of $420.00 is enclosed for claims added to this Amendment D. The Commissioner is hereby authorized to charge any additional fees which may be required to Deposit Account No. 19-1345.

Respectfully submitted,



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